A remedy for the Achilles tendon of echocardiography?

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Echocardiography remains the modality of choice for diagnosis and follow-up in heart disease as it is relatively risk-free, mobile (even portable) and – importantly – cheap and therefore widely available. Although improvements in ultrasound technology have resulted in more accurate, reproducible, faster and user-friendly methodologies towards the morphologic and functional evaluation of the heart, to date, no robust ultrasound methodology is available for clinical routine to determine tissue viability. As tissue viability is an important boundary condition for treatment options and treatment outcome, patients are often referred – for this reason – to other imaging modalities such as MRI or PET. Viability imaging could therefore be considered the Achilles tendon of echocardiography.

Not surprisingly, it has thus been an active research topic for decades and new approaches to assess viability were proposed hand-in-hand with evolutions in ultrasound imaging technology. Although it was demonstrated that irreversibly damaged, i.e. non-viable, myocardium is thicker than dysfunctional but viable, i.e. stunned, myocardium early after reperfusion of acute myocardial infarctions [1], most methodologies did not directly measure tissue properties but rather focused on assessing the variable functional reserve of stunned versus infarcted myocardium. For example, stress echocardiography has demonstrated that stunned segments show preserved contractile reserve while infarcted segments do not [2]. Similarly, Doppler myocardial imaging [3] and speckle tracking echocardiography [4] during stress echocardiography provide a similar differentiation but in a more quantitative manner. In the eighties, it was demonstrated that the cyclic variation of the integrated backscatter could equally differentiate stunned from infarcted myocardium [5]. Finally, the assessment of myocardial perfusion using ultrasound contrast echocardiography has shown to differentiate both ischemic substrates [6].

Without doubt, the major technological evolution of ultrasound imaging in the last decade has been fast imaging and likely this will be similar in the decade to come. Although the frame rate of echocardiography has always been adequate to look at the gross motion of the heart, it is not until recently that imaging strategies were proposed that allow imaging the heart at very high temporal resolution with frame rates going up to 10.000Hz. Although it may seem unnecessary to image the heart at this time scale, it does allow extracting new information that could be of (added) diagnostic value [7].

In this issue of JACC Cardiovascular Imaging, Pernot and colleagues report on an experimental animal study demonstrating the potential use of one of these new parameters in differentiating infarcted from stunned myocardium. More specifically, the authors used ultrafast imaging to measure the propagation speed of shear waves, acoustically induced in the myocardium, thereby estimating local myocardial stiffness. Interestingly, this methodology characterizes the native tissue (mechanical) properties rather than the functional consequences of viability. The authors convincingly

demonstrated that stunned myocardium returns to near normal elastic properties within minutes after reperfusion while infarcted myocardium continues to stiffen after reperfusion. Importantly, these findings were not only obtained with the novel ultrafast imaging approach but validated by an independent, invasive estimate of local stiffness.

The findings of Pernot et al. are perfectly in line with those of Pislaru et al. [Pislaru04]. Indeed, on the one hand, Pislaru and colleagues measured the response of ventricular wall thickness on changing left ventricular pressure as a result of vena cava occlusion; on the other hand, they measured the local tissue deformation (i.e. strain) as a result of left ventricular pressure increase during atrial contraction. Both approaches allowed estimating local tissue stiffness and demonstrated that non-viable myocardium is stiffer than viable myocardium early after reperfusion.

An important improvement of the ultrafast imaging methodology proposed by Pernot et al. is that it provides *absolute* stiffness measures. Indeed, although strain induced by atrial contraction was different for stunned and infarcted myocardium in an experimental animal setting [Pislaru04], translating their methodology to clinical practice is difficult as many confounding factors can result in equally low local strain values during atrial contraction: global LV dilation; local LV shape and wall thickness changes that are in turn related to infarct size, location and transmurality; changed LV compliance; poor left atrial function; and others. Moreover, assessing myocardial stiffness in absolute value (i.e. in kPa) - as done by Pernot et al. – not only implies that these confounding factors can be mostly neutralized but also that local myocardial stiffness can be compared between individuals. As such, it becomes possible to define clear threshold values to differentiate viable from non-viable myocardium without the need to correct for confounders. In this context, it appears very promising that the stiffness of non-viable myocardium was an order of magnitude different from that of normal / viable myocardium (12.1 versus 2.3kPa respectively) and that the range of normal values was very narrow (standard deviation 0.4kPa).

Does this methodology then finally solve the weak spot of echocardiography? Did we finally get a robust and reliable ultrasound methodology to predict functional recovery of segments after reperfusion of an acute myocardial infarction as a first application of viability imaging? Unfortunately, the answer to these questions remains negative for clinical as well as technological reasons. Indeed, in clinical practice, the range of ischemic substrates encountered is more diverse than the two extreme situations created in this animal study, i.e. stunned versus transmural infarction. In particular, non-transmural infarctions will equally often be encountered, resulting in a more heterogeneous substrate that might lead to intermediate stiffness values when measured at the segmental level thereby complicating the viability classification. Of course, one could hope that the spatial resolution of the ultrafast imaging approach is sufficiently high in order to make a stiffness estimate at different depths across the wall leading to a stiffness image that might be read very similar to an MRI delayed enhancement image. This might be the case as the team of Pernot previously demonstrated that the shear wave speed can be measured at different depths across the myocardial wall in order to determine local fibre orientation based on the fact that these shear waves travel faster along the fibre than across them [8]. Unfortunately, this implies that a change in shear wave speed across the wall cannot simply be related to local stiffness as local fiber orientation should be considered. Although this confounder may be corrected for, it does complicate classification.

A more fundamental problem of the proposed methodology might be the technological challenges related to its translation to the clinical setting. Indeed, inducing shear waves in the anterior wall of an open-chest animal preparation and imaging their propagation at ultra-high frame rate by a linear array transducer in direct contact with the heart is quite distinct from inducing a shear wave in any

other wall of a closed-chest patient and imaging its propagation through a narrow acoustic window for the following reasons: i) the induction of shear waves requires insonification of the tissue with sufficient acoustic energy in order to be able to push the tissue away from the transducer via its acoustic radiation force – this is not obvious further away from the transducer due to attenuation particularly when using a transducer with a small footprint (i.e. a transthoracic phased array) that limits focusing; ii) for the shear wave to be generated and detected using the same (2D) transducer position as required by the presented methodology, the only echocardiographic view that can be used is the parasternal one – this implies that stiffness can only be measured in the anterior and posterior wall segments; iii) ultrafast imaging is facilitated by linear arrays with large footprint and therefore an intrinsic large field of view – translation to phased arrays is not straightforward although solutions are being proposed.

Despite the challenges in translating the proposed methodology to the clinical setting, this study convincingly demonstrates the potential of stiffness imaging of the heart. Although it may not allow mapping local stiffness (changes) bedside in its present implementation, new technological advances may solve this. Moreover, even if local stiffness maps remain unfeasible, the technique presented may still be of great value for example to determine the aetiology of diastolic heart failure by obtaining a quantitative estimate of (local) ventricular compliance. It is thus clear that this study is just the tip of the iceberg and that many exciting applications of ultrafast cardiac imaging are yet to come. Without doubt, ultrafast cardiac imaging will further strengthen ultrasound as the cardiac imaging modality and it is again Paris that finds the weak spot of Achilles; this time not to murder him but rather to help making him truly invincible.

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